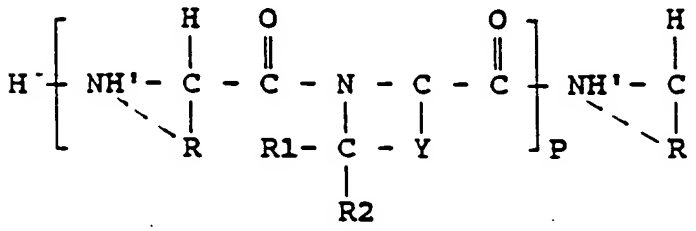
Reclaim

1. An inhibitor compound, having the structure

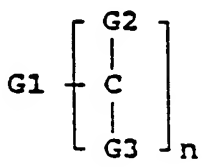
Group I - Group II

where Group I has the structure:



wherein each R, independently, is chosen from the group consisting of the R groups of an amino acid including proline; each broken line, independently, represents a bond to an H or a bond to one said R group, and each H' represents said bond or a hydrogen; p is an integer between 0 and 4 inclusive;

or Group I has the structure:



where n is between 0 and 3 inclusive,

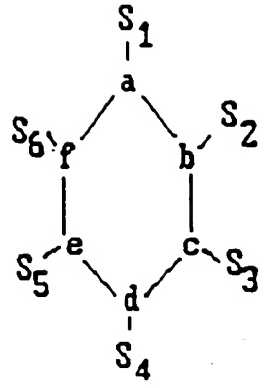
each G2 and G3 independently is H or C1 - 3 alkyl,

G1 is NH_3, $NH-C(=NH_2)-NH_2$, or

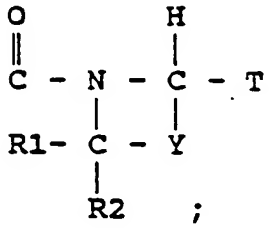
NG_4, where G4 is $C(-G_5)-G_6$

where G5 and G6 can be NH, H, or C1 - 3 alkyl or alkenyl with one or more carbons substituted with a nitrogen; provided that G1 bears a charge and G1 and Group II do not form a covalently bonded ring structure at pH 7.0;

or Group I has the structure:



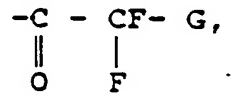
where one or two of said a, b, c, d, e, and f is N and the rest are C, and each S1 - S6 independently is H or C1 - C3 alkyl; where Group II has the structure:



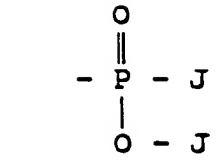
;

T is a group of the formula:

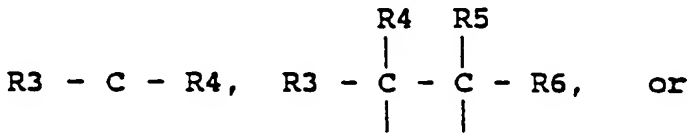
, where B is boron and each D1 and D2, independently, is a hydroxyl group or a group which is capable of being hydrolysed to a hydroxyl group in aqueous solution at physiological pH; a group of the formula:

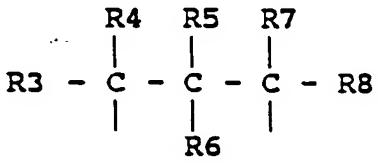


where G is either H, F or an alkyl group containing 1 to 20 carbon atoms and optional heteroatoms which can be N, S, or O; or a phosphonate group of the formula:



where each J, independently, is O-alkyl, N-alkyl, or alkyl, each said O-alkyl, N-alkyl or alkyl comprising 1 - 20 carbon atoms and, optionally, heteroatoms which can be N, S, or O; said T being able to form a complex with the catalytic site of a dipeptidyl-aminopeptidase type IV (DP IV) enzyme;

Y is  , or



and each R1, R2, R3, R4, R5, R6, R7, and R8, separately is a group which does not significantly interfere with site specific recognition of said inhibitory compound by said DP IV, and allows said complex to be formed with said DP IV.

Prelim

7. The compound of claim 1, wherein T is a boronate group.

8. The compound of claim 1, wherein T is a phosphonate group or a trifluoroalkyl ketone group.

9. The compound of claim 1 wherein each R1 - R8 is H.

5. The compound of claim 1 or 2 wherein each R1 and R2 are H, and each Y is CH_2 - CH_2.

6. The compound of claim 5 wherein each R is independently chosen from the R group of proline and alanine.

7. The compound of claim 1, wherein said compound has a binding or dissociation constant to said DP IV of at least 10^{-9}M.

8. The compound of claim 1, wherein said compound has a binding constant to said DP IV of at least 10^{-8}M.

9. The compound of claim 1 admixed within a pharmaceutically acceptable carrier substance.

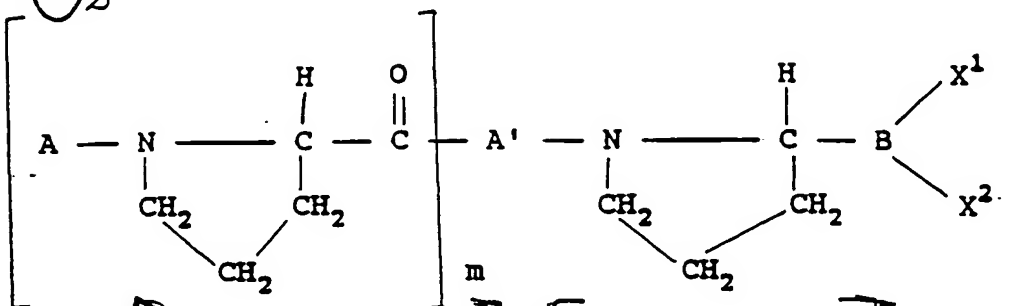
10. The compound of claim 1 wherein, each D1 and D2 is, independently, F or D1 and D2 together are a ring containing 1 to about 20 carbon atoms, and optionally heteroatoms which can be N, S, or O.

11. A method for inhibiting DP IV in a mammal, comprising administering to said mammal an effective amount of a compound of claim 1.

12. The method of claim 11 wherein said amount is 1 - 500 mg/kg/day.

Claims as filed

(Amended) 13. An inhibitor of DP-IV, having the structure:



wherein m is an integer between 0 and 10, inclusive; A and A' are L-amino acid residues such that the A in each repeating bracketed unit can be a different amino acid residue; the C bonded to B is in the L-configuration; the bonds between A and N, A' and C, and between A' and N are peptide bonds; and each X^1 and X^2 is, independently, a hydroxyl group or a group capable of being hydrolysed to a hydroxyl group at physiological pH.

14. The inhibitor of claim 13 wherein A and A' are independently proline or alanine residues.

15. The inhibitor of claim 13 wherein m is 0.

16. The inhibitor of claim 13 wherein X^1 and X^2 are hydroxyl groups.

17. The inhibitor of claim 13 wherein said inhibitor is L-Ala-L-boroPro.

18. The inhibitor of claim 13 wherein said inhibitor is L-Pro-L-boroPro.

amended 2/26/97

See 7008

m=0

cancelled 2/26/97 cancel

Cancelled Non elected L-Pro-L-boroPro

Cancelled Prelim

19. A method for inhibiting DP-IV in a mammal, comprising administering to said mammal an effective amount of a compound of claim 13.

20. The method of claim 19 wherein said amount is 1 mg/kg of said mammal per day to 500 mg/kg of said mammal per day.